Asthma severity, allergy and lung function during young middle life in subjects with asthma in childhood

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Abstract The further course of asthma severity, lung function, bronchial hyperresponsiveness (BHR) to cold air challenge (CACH), clinical allergies and allergic sensitization in young middle adulthood was studied in a cohort of 55 subjects with childhood asthma. All subjects (27 females) have attended all five previous and the current follow-up visit, undertaken at a mean age of 35 years. Twelve subjects (22%) reported no current asthma, 28 (51%) mild/intermittent, and 15 (27%) moderate/severe asthma. Asthma severity changed little in the individual subjects over the last 5-year period. Females continued to have higher asthma severity scores than the males, but the previously noted lower resting and post-bronchodilator % predicted FEV₁ in females was not confirmed now. Pathological BHR to CACH tended to be more common among the males. Forty-four subjects were still allergic to animal danders and 35 to pollens. Sensitization rates (skin prick test or RAST) were similar to those recorded 5 years earlier and there was no clear evidence of tolerance developing. Five subjects have never shown evidence of allergy or sensitization. The extent of sensitization to animal danders showed statistically significant relationships to asthma severity and BHR to CACH. Social development and professional careers continued to be good.

INTRODUCTION

We have previously described the course of asthma in a cohort of 55 asthmatic schoolchildren recruited at a mean age of 9 years and then prospectively followed-up on five occasions to the mean age 30 years (1,2). We reported the course of clinical asthma severity, allergies, lung function and social adaptation. Asthma severity improved from childhood to adulthood but after adolescence asthma continued to improve only among the males. In most subjects, clinical allergies and sensitization (assessed by skin prick tests and RAST) to inhaled allergens persisted into adulthood. Lung function as determined from percent predicted FEV₁ was higher in females than in males over the first two follow-ups, but the reverse was found over the subsequent visits. At the last follow-up significant relationships were found between the degree of bronchial hyperresponsiveness (BHR) to cold dry air challenge (CACH) and asthma severity and to the extent of sensitization to furred animals. The social prognosis was good, judged by, e.g. marital status, educational level and employment rate. The use of health care facilities and school absence were high in childhood but in adulthood hospital admissions and sick listing were rare.

We have now, 5 years later, performed a new follow-up in all 55 subjects when their age was on average 35 years, aiming to see if asthma severity and lung function have changed during young middle adulthood. We were also interested in seeing if sensitization to inhaled allergens and clinical allergy had decreased, and if the previously noted associations between allergic sensitization and asthma severity and BHR persisted. Finally, we wanted to see if the higher asthma severity scores and worse lung function remained among the females.

STUDY SUBJECTS

The study subjects constituted a group of 55 adults with the mean age of 35 years (range 30–40 years). The cohort was initially selected randomly among asthmatic children visiting an outpatient pediatric unit in a central...
hospital with the intention to include half boys and half girls (for gender comparison) and to include patients who would be at least 7 years old at the planned first follow-up (to be able to perform spirometry). Asthma was defined as a history of three or more episodes of wheezing, confirmed by a physician at least on one occasion. One girl died in an asthma attack at the age of 16 years. All the remaining subjects (28 males and 27 females) have attended all follow-ups, including the current, sixth, follow-up. The recruitment visit (designated I) was performed at the mean age of 9.4 years and the follow-up visits (designated II–VII) were done at the mean ages of 11.5, 13.6, 17.2, 24.3, 30.0 and 35.0 years. The ages of the females and the males were similar at all visits. The visits were timed to allow the patients to be in optimal condition and outside the pollen season.

Onset of wheezing was before 2 years of age in 47% of the subjects (retrospective data) according to information obtained at visit I, supported by health records, and confirmed at visit II. All subjects had experienced at least one episode of wheezing the year before visit I. Six of the 55 patients never reported any clinical allergy to pollens, furred animal danders or food and in five of them all tests for sensitization were negative at all the previous follow-up visits.

During childhood 84% lived in one-family houses and 44% lived in rural areas. During childhood about half of them had indoor furred animals and 56% of the subjects were exposed to domestic tobacco smoke. At the previous visit six women but no men were tobacco smokers.

**METHODS**

**Definitions**

History was taken using a standardized interview questionnaire emphasizing the frequency and severity of asthmatic symptoms, allergic reactions, other atopic manifestations, and social and environmental issues. One of the authors (B.K.) participated in the evaluations throughout the study. Asthma severity was estimated according to the frequency of wheezing (score 0–3) and the degree of medication (score 0–3) reported from the 12-month period prior to the follow-up visits, which give a total asthma score of 0–6. Clinical allergy was estimated by questioning the occurrence of clinical reactions to pollens (during the two seasons prior to the follow-up), danders (the year prior to the follow-up) or food. Further details of the definitions are given in the previous reports (1,2).

**Skin prick tests**

The skin prick tests (SPT) were performed using the same technique and allergen extracts as used at the previous follow-up and the same nurse performed them. A weal with a mean diameter (half the sum of the largest diameter and its mid-point perpendicular) of more than 3 mm was denoted positive. Histamine solution (10 g l⁻¹) was used as a positive reference. The reactions at the penultimate visit (visit VI) and the last visit (VII) were compared for the following allergens: birch (Betula verrucosa), grass (Phleum pratense), cat (Felis domesticus), dog (Canis domesticus), horse (Equus cabellus), mites (Der fariinae and Der pteronyssinus). The extracts (ALK, Copenhagen, Denmark) were used in concentrations of 10 heparin equivalent potency (HEP), corresponding to 10 000 biological units ml⁻¹. The precision of the SPTs was evaluated by duplicate testing. The coefficients of variation (expressed as percentages of the mean weal diameter) at visit VI and VII, respectively, were 14 and 16% for histamine, 23 and 21% for birch, 19 and 19% for grass, 15 and 21% for dog, 24 and 25% for horse, 24 and 20% for cat, 14 and 18% for Der fariinae and 20 and 10% for Der pteronyssinus. The mean diameter of the histamine weal at visit VI (6.7 mm, range: 4.5–90) was significantly higher than that at visit VII (6.3 mm, range: 4.5–8.5; P = 0.005). In the calculations and presentations the diameters of the weal produced by allergens were related to the diameter of the histamine weal, which implies that the value 1.0 of a patient corresponds to a weal with the same size as the histamine weal of that patient.

**Serum levels of total and specific IgE**

All analyses were done on sera stored frozen from visits VI and VII on the same occasion in the Department of Clinical Chemistry/Lab Novo-Calab, Central Hospital, Skövde, Sweden using the Phadebas CAP method (Pharmacia Diagnostica, Uppsala, Sweden). The concentrations (kU ml⁻¹) of antibodies to the following antigens were compared: birch, timothy, cat, dog, horse, Der fariinae and Der pteronyssinus. The coefficient of variation was 9–10% for total IgE, 6–10% for the two pollens, horse and cat, 12% for dog and 16% for the two house dust mites. RAST concentrations ≥0.35 kU ml⁻¹ were regarded as positive. When comparing the relationship between the extent of sensitization to animal danders and bronchial hyperresponsiveness concentrations corresponding to RAST class 2 or more (≥0.70 kU ml⁻¹) were regarded as positive.

**Lung function tests and bronchial challenge**

At the current visit spirometry, body plethysmography and isocapnoic cold dry air challenge (CACH) were performed in the same laboratory with the same staff, using the same equipment and protocol as that at visit VI (2). The participants refrained from short-acting β₂-agonists and inhaled corticosteroids for 6 h, long-acting β₂-agonists for 24 h and antihistamines for 72 h prior to lung
function testing. Dynamic and static lung volumes were recorded in a constant volume body plethysmograph (Jaeger Masterscreen, Erich Jaeger AG, Wurzburg, Germany). At visit VI 53 subjects and at the current visit all 55 subjects went through CACCh which consisted of 4 min of hyperventilation of cold, –15°C, dry air at 75% of the predicted maximum voluntary ventilation (26 × baseline FEV₁ 1 min⁻¹). A fall in FEV₁ of 10–19% was regarded as an abnormal minor airway reaction, and a fall in FEV₁ of 20% or more was regarded as a major airway reaction. After CACCh the patients inhaled a 5 mg ml⁻¹ solution of salbutamol for 2 min from a jet nebuliser (Maxin; Clinova Medical AB, Malmö, Sweden) and 15 min later spirometry was performed in the same way as for baseline recordings. All spirometric volumes were expressed at BTPS and as percentages and standard deviation (SD) scores from Swedish reference values (3,4).

Data analysis and statistics
Equality between non-paired proportions was assessed with the χ²-test or the Fisher exact test if an expected table cell value was less than five. The McNemar’s test was used for paired observation, e.g. assessing the change between visit VI and VII. For sets of score data or sets of data without a normal distribution equality was assessed with the Mann–Whitney test for unpaired data and the Wilcoxon matched pairs sign rank test for paired data. For other sets of data the unpaired or paired Student’s t-test was used. Correlation between the values of total IgE obtained at visit VI and VII was estimated with the Spearman’s rho.

RESULTS
Asthma severity
The mean total asthma score changed from 1.9 at visit VI to 1.6 at visit VII among the males (n.s.) and from 2.3 to 2.4 among the females (n.s.). At visit VI, the difference between the females and males did not reach statistical significance, but at the last visit the total asthma score was significantly higher (P = 0.044) among the females than the males. This difference at the last follow-up resulted mainly from a significantly lower medication score in the males (0.7) than in the females (1.2; P = 0.024).

The number of subjects with various total asthma scores at visits VI and VII is shown in Fig. 1. The slight changes between the two visits were not significant. Seven of the 12 subjects (nine males) with score 0 at visit VII had an asthma score of 0 also at visit VI. The remaining five subjects had a score of 1 or 2 at visit VI. No asthma symptoms or mild asthma (score 1 or 2) were reported by 69% of the subjects at visit VI and by 73% at visit VII. Seventeen subjects (eight males) scored 3–6 at visit VI and 15 (six males) at visit VII, all of which scored 3–6 at visit VI.

Two males and one female attended for emergency care for asthma during the 12-month period prior to the last visit. Two males had been sick-listed on a single occasion for about a week and one female had been admitted to hospital due to asthma for a short stay during the last year.

None of the 40 subjects with an asthma score of 0–2 medicated regularly for asthma at the current visit. Nine of the 15 patients (6 males) with a total asthma score of 3–6 used asthma medication continuously. Eight subjects used inhaled corticosteroids (ICS) and four reported additional regular use of inhaled long-acting β₂-agonists.

Clinical allergy
Forty-four subjects (24 males) reported current allergy to furred animals at visit VII, compared to 42 subjects (22 males) at visit VI. One of the latter 42 subjects was free from this allergy between visits VI and VII and another three subjects had acquired or re-acquired such allergy. The time from the first prospectively recorded occurrence of allergy to animal danders in currently allergic subjects was more than 20 years in 38 of the 44 subjects (86%), more than 25 years in 27 subjects (61%), and less than 10 years in only one currently allergic subject.

Thirty-five subjects (20 males) reported current allergy to pollens at visit VII, compared to 29 subjects (14 males) at visit VI. One of the latter 29 subjects had lost the pollen allergy and seven subjects had acquired or re-acquired pollen allergy between visits VI and VII. The time from the first prospectively recorded report of pollen allergy in currently allergic subjects was more than 20 years in 29 of the 35 subjects (83%), more than 25 years in 19 subjects (54%), and less than 10 years in only four currently allergic subjects (7%).
The same 21 subjects (nine males) reported allergy to fruit, berries, nuts or peanuts both at visit VI and VII. Sixteen subjects reported allergy to nuts (hazel nut, walnut or Brazil nut) and three subjects reported allergy to peanuts (all three were also allergic to nuts). Two subjects reported general anaphylactic symptoms (one to nuts and one to peanuts) and they were both equipped with disposable epinephrine syringes for emergency use. The remainder reported only oral allergy symptoms after intake of nuts or peanuts. Two subjects reported allergy to fish, one to shellfish and one to raw eggs.

Sensitization

The number of subjects with positive SPT or RAST to various inhaled allergens at the two visits is shown in Table I, which also displays the high retention rates. The time from the first prospectively recorded SPT to cat dander was more than 20 years in 35 of the 41 subjects (85%) with a currently positive SPT and more than 25 years in 20 subjects (49%). The time from the first prospectively recorded SPT to timothy pollen was more than 20 years in all 36 subjects (100%) with a currently positive SPT and more than 25 years in 19 subjects (53%).

Figures 2 and 3 show the histamine-related SPT weal diameters and the IgE concentrations for birch, timothy, dog and cat at visits VI and VII. Among the subjects with a positive SPT to timothy at visit VI there was a significantly ($p < 0.001$) smaller histamine-related timothy weal size at VII vs. VI. No significant changes were seen for the other allergens. Among the subjects with a positive RAST to any inhaled allergen at visit VI small but statistically significant reductions in median concentrations of specific IgE were seen for timothy ($p < 0.001$), dog ($p < 0.001$), cat ($p < 0.001$) and horse ($p = 0.004$).

The magnitudes of the SPT weal and the RAST concentrations to the two house dust mite allergens (D. pteronyssinus and D. farinae) were lower than those of other

### Table 1

<table>
<thead>
<tr>
<th>Test findings</th>
<th>Visit VI</th>
<th>Visit VII</th>
<th>From visits VI to VII</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>Adopted</td>
</tr>
<tr>
<td>Pos. SPT to:</td>
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<td></td>
<td>n</td>
</tr>
<tr>
<td>Timothy</td>
<td>37</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>Birch</td>
<td>35</td>
<td>37</td>
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<td>27</td>
<td>0</td>
</tr>
<tr>
<td>Dog</td>
<td>39</td>
<td>42</td>
<td>5</td>
</tr>
<tr>
<td>D. pteronyssinus</td>
<td>6</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>D. farinae</td>
<td>9</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Pos. RAST to:</td>
<td></td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Timothy</td>
<td>36</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>Birch</td>
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<td>35</td>
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</tr>
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</tr>
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<td>38</td>
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<td>12</td>
<td>2</td>
</tr>
<tr>
<td>D. farinae</td>
<td>11</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

The number of subjects with positive skin prick test (SPT) or RAST at visits I (mean age 30 years) and at visit VII (mean age 35 years) are given. The number of subjects adopting or losing test reactivity between the visits and the retention rates are also given.
allergens in the subjects with a positive test. The 10 patients who retained a positive RAST to mites from visit VI to VII had positive RAST to the two mites at both the occasions.

The median serum concentration of total IgE at the current visit (92 kU l⁻¹; inter-quartile range: 36–170 kU l⁻¹) was significantly lower (p = 0.004) than that at visit VI (104 kU l⁻¹; inter-quartile range: 45–209 kU l⁻¹). The correlation (rho) between the values at visit VI and VII was 0.92 (p < 0.001).

**LUNG FUNCTION AND BRONCHIAL HYPERRESPONSIVENESS**

The number of subjects with pathological findings at lung function testing or CACCh at visits VI and VII is given in Table 2. The single most common pathological finding at both visits was pathological BHR to CACCh. There were no significant gender differences in number of subjects with abnormal findings of any kind at the two last visits. At the current visit, however, BHR to CACCh tended to be more frequent finding among the males (18/28 subjects; 64%) than among the females (10/27; 37%; p = 0.064). While baseline and post-β₂-agonist percent predicted FEV₁ tended to be lower among the females than the males at visit VI, this difference had disappeared at visit VII [Fig. 4(A) and (B)].

Resting lung function, BHR and reversibility of FEV₁ after β₂-agonist inhalation are given in Table 3 separately for three subgroups of the participants separated on the basis of total asthma scores. The 15 subjects with asthma scores 3–6 had significantly lower spirometry results and significantly more pronounced BHR to CACCh than the remainder.

The relationships between asthma severity scores and BHR to CACCh and between BHR and extent of sensitization to animal danders are shown in Figs. 5 and 6. There

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**Fig. 3.** Serum concentrations of specific IgE (RAST kU l⁻¹) to four inhaled allergens at visits VI and VII in subjects with positive RAST at visit VI.

**Fig. 4.** Baseline % predicted FEV₁ [Fig 4(A)] and post-bronchodilator % predicted FEV₁ [Fig 4(B)] given for males and females separately over all six follow-up visits.

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**TABLE 2.** The number of subjects with pathological findings at lung function testing or CACCh (cold air challenge) at visits VI and VII.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Visit VI n</th>
<th>Visit VII n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline FEV₁ &lt; pred. mean -L64 RSD</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Baseline FEV₁/VC% &lt; pred. mean -L64 RSD</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Baseline RV/TLC &gt; pred. mean + L64 RSD</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>≥ 10% increase in FEV₁ after β₂ therapy</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Fall in FEV₁ ≥10% after CACCh*</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Fall in FEV₁ ≥20% after CACCh*</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Any abnormality</td>
<td>29</td>
<td>33</td>
</tr>
</tbody>
</table>

(RSD = residual standard deviation; RV = residual volume; TLC = total lung capacity).

*53 subjects were tested at visit VI and all 55 at visit VII.
was a significant relationship between asthma severity and the degree of BHR \((P < 0.001; \text{Fig. 5})\). Likewise, there was a significant overall relationship between the number of positive RAST to animal danders and BHR \((P = 0.034; \text{Fig. 6})\).

**Social aspects**

All subjects were employed when attending the current visit, at a time when the Swedish unemployment rate was approximately 4%. At the previous visit five subjects were unemployed but at that time the national unemployment rate was approximately 10%. At the current visit 47 subjects were married or lived in a marriage-like relationship (45 subjects at visit VI) and 40 subjects had children (27 subjects at visit VI). According to the interviews about half of their 84 children had atopic dermatitis, asthma or allergy to pollen, danders or food.

At the current visit 20% of the participants lived in rural areas and 73% lived in one-family houses. Seven subjects (two males) had indoor furred animals (dog and/or cat) of whom four reported allergy to furred animals and five were sensitized to animal allergens. Five women but none of the males were currently tobacco smokers (5–15 cigarettes daily) and eight men took tobacco snuff. At the previous visit six subjects (all women) were tobacco smokers.

At the current visit 26 (14 males) of the participants (47%) reported regular physical sport activities at least once a week as compared to two-thirds at the previous visit.

**DISCUSSION**

The current follow-up of this cohort was performed 5 years after the previous visit. The mean age of the participants was 35 years, and the same broad test protocol was used. The previously noted trend towards higher asthma scores among the females than among the males in adult life was stronger at this follow-up than at the
previous (I). However, on the whole asthma severity changed little over the 5-year period. The significant lung function impairment observed among the females at the previous follow-up could not be confirmed this time. Another two findings deserve attention. Firstly, the study demonstrated that the previously recorded high rates of clinical allergies and sensitization to animal danders and pollens in adult life (I) persisted through young middle life. Secondly, indirect BHR as measured by the response to CACh continued to show significant correlation to the extent of sensitization to animal danders and to asthma severity at this follow-up. These findings indicate that IgE-mediated hypersensitivity to ubiquitous perennial allergens continues to be important for asthma severity through middle adulthood in former asthmatic children.

It can be argued that the general applicability and relevance of the findings and conclusions drawn from the present cohort is limited due to the relatively small number of subjects in the cohort. We believe the current follow-up to be unique and powerful because it comprises six follow-up visits from childhood to young middle adulthood, all attended by all subjects, except one who died from asthma at the age of 16 years. It is obvious that several stations and high attendance rates are important in asthma follow-up studies when delineating the course of the disease. Furthermore, a full picture of the disease was obtained at all follow-up stations as most aspects of the disease were assessed: disease severity by interviews, lung function, clinical allergies, sensitization to a range of relevant allergens, as well as the influence of asthma on social life. Finally, this cohort was selected randomly among children attending a pediatric outpatient clinic during the 1970s with the aim of including half boys and half girls. Therefore, we feel that the course of asthma in this cohort may give a good and representative picture of the course of the disease among Swedish school children born in the 1960s and who were diagnosed with asthma by a pediatrician.

A few other asthma follow-up studies reaching into young middle adulthood have included more patients (5–II). One recently reported cohort from the Netherlands consisted of initially 119 patients with childhood asthma recruited from a hospital clinic (78). They were investigated once during childhood and 101 of them were followed-up twice during adulthood at age 22–32 years and 32–42 years; but the study reported mainly childhood risk factors for asthma outcome in adulthood (7, 8). Another recently reported follow-up study from Melbourne, Australia, consisted of 295 children with asthma recruited by parental response to a questionnaire at the age of 7 years and an additional group of 83 children with severe asthma, incorporated into the initial cohort at the age of 10 years (9–II). Out of the 378 children 327 (87%) were reviewed at least one occasion at the age of 14, 21, 28, or 35 years (II).

**Little change in asthma severity during young middle life**

Baseline lung function and airway response to CACh did not differ between the group of 12 subjects who reported no current asthma and the 28 subjects reporting mild intermittent asthma (total asthma scores 1 or 2) indicating that airway disease actually differed little between these subgroups. Several of the subjects belonging to these severity categories had migrated between the categories between the previous and the last visit. While seven of the 12 subjects without current asthma scored zero also at the previous visit, the remaining five scored 1 or 2 then. Furthermore, 30 of the 40 subjects scoring 0–2 at the current visit scored similarly at all three visits in adult life. Among the 15 subjects with moderate or severe asthma (scores 3–6) baseline lung function and BHR to CACh were significantly worse than among the 40 with none or mild asthma, confirming that these 15 subjects indeed represent a subgroup with worse outcome. Ten of them had been classified belonging to that severity category at all three visits during adulthood. In the Melbourne study (II) the participants tended to move toward one or the other extreme of asthma severity with increasing age, but throughout adulthood, over three follow-ups, the group with no recent or infrequent asthma varied only between 52 and 56% and the group with frequent or persistent asthma varied between 43 and 48% only. These findings (II) indicate a similar stable asthma course during adulthood as seen in the current study.

Childhood asthma appears to regress completely in a minor proportion of the sufferers only. In the current study merely five of the 12 subjects who scored zero at the last follow-up fulfilled the criteria of absence of asthma and medication at all three follow-up visits in adulthood and another two participants reported no asthma symptoms or medication at the two last visits. Three of these seven subjects, however, showed an abnormal airway response to CACh at the current visit, which implies that the freedom of symptoms may be temporary only.

Generally, the long-term outcome of childhood asthma seems to be favorable as judged from this cohort, since 73% of the subjects had no or only mild symptoms in middle adulthood. In the Melbourne study 56% of the subjects had no current asthma or only infrequent symptoms at the age of 35 years (II). This somewhat less favorable outcome may reflect the influence of the added group of severe asthmatics. In the Dutch follow-up of 119 asthmatic children 101 were investigated at a mean age of 26 years (range 22–31 years) (6). Only 43 subjects had current asthma symptoms and 29 of these were taking asthma medication (6).

Not only clinical asthma severity seemed to be stable in middle adulthood in the current cohort, but the bronchial response to CACh, which was tested in 53 partici-
pants at both of the last two visits, also seemed to be rather stable as 18 of 24 subjects with an abnormal reaction anytime had an abnormal response at both visits. A similar pattern was seen for resting lung function.

Only five of the 12 subjects with a fall in FEV1 of at least 20% after CACh used inhaled corticosteroids regularly. Among the 16 subjects with an FEV1 reaction between 10 and 19% none took inhaled steroids, while three of the 27 remaining used such medication. Out of the seven subjects with pronounced BHR to CACh and who did not use ICS, four (all males) reported mild or no asthma. These findings suggest that asthma was undertreated in several subjects, and that asthma symptoms were poorly perceived by some of these subjects. The findings also point to the need and importance of scheduled regular check-ups of adult subjects with asthma.

### Little change in allergy during young middle life

The high retention rate of clinical allergies and sensitization to inhaled allergens from childhood to adulthood previously seen persisted in young middle life. Also clinical allergies to food such as berries, fruits, nuts and peanuts remained stable between the last two visits. We derived advantage from having stored frozen sera from the previous visit to estimate the change in serum concentrations of IgE antibodies to various inhaled allergens over the last 5 years. There was a statistically significant decrease in the RAST levels for some of the allergens but the reductions were small. A significant but slight decrease was also observed for the SPT reaction to one of the allergens (timothy). These changes might predict a future development of tolerance, but this remains to be investigated in the future. The RAST levels and the magnitudes of the skin reactions were still very high and there was no conclusive evidence of development of tolerance either judged clinically or by careful estimation of sensitization.

The high retention rates of clinical allergies and sensitization, particularly to furred animals, and the association between sensitization and BHR, have several implications. Because the allergens from cats and dogs are present in most public environments (12,13) avoidance is not possible for those who have become allergic. Protection from exposure to animal danders is consequently difficult to accomplish, and BHR and asthma severity may be maintained due to daily exposure to these allergens outside the home. Immunotherapy to cat and dog allergens in order to induce tolerance could be motivated in children with moderate or severe asthma as these allergens appear to determine asthma severity even in adult life. The possible beneficial long-term effects of such intervention need to be assessed in prospective controlled studies.

The proportion of non-allergic subjects in the adult asthma population is commonly believed to be much higher than in asthmatic children. Only five subjects persisted to have a non-allergic asthma all through from childhood to young middle adulthood in our cohort. This finding in combination with the fact that only a few of the other 50 subjects had lost their allergies would suggest that the majority of adult asthmatics with non-allergic asthma in a general population have become asthmatic after childhood. To our knowledge, no long-term studies have been reported previously on the course of both clinical allergies and sensitization from childhood to adulthood and further during adulthood in asthmatic subjects.

### Good social outcome

Living conditions and family life do not seem to differ in this cohort from those in a more general Swedish population and all participants were employed at this follow-up. None of the participants reported that they ever had to resign from a job or change education due to their asthma, while a few had changed professional direction due to their atopic eczema. As may be expected with increasing age and family responsibilities a more sedentary life style was adopted since the previous follow-up, but half of the subjects still exercised regularly. A large proportion of the offspring was reported to have atopic disease or allergies confirming the strong hereditary influence on these conditions.

### Higher asthma scores in the females

The total asthma severity scores were significantly higher in the females than in males at the current follow-up, due to higher asthma medication scores in the women. Some other findings suggest, however, that asthma was not more severe in women. In contrast, to the findings at the previous visit, baseline and post-bronchodilator percent predicted FEV1 were not lower in females this time. Furthermore, the airway response to CACh was pathological in almost twice as many males as females at the current follow-up (64 vs 37%), a finding that did not quite reach statistical significance. If anything, the CACh results would indicate that asthma was undertreated in some of the males.

In summary, asthma severity, lung function and BHR changed little during middle adulthood in this cohort of subjects with asthma in childhood. Almost three-quarters of the subjects reported only mild or no asthma symptoms, but only a small percentage appeared to be completely free from asthma, suggesting that asthma is indeed a life-long condition. Sensitization to perennial ubiquitous allergens continued to influence asthma severity and there was no evidence of development of
tolerance. Females reported slightly worse asthma than males, but their lung function was similar and BHR tended to be worse in males. On the whole, lung function was well preserved and within normal limits in most subjects in young middle life. Asthma did not unfavorably affect social adaptation or professional career.

REFERENCES


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